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Ndukwu C
Onah S
Ebenebe J
Osuorah D

Clinico - demographic factors associated with diarrhoeal disease outcome in under-five children: A Nigerian tertiary hospital experience

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Ndukwu C (✉)
Onah S, Ebenebe J
Department of Paediatrics,
Nnamdi Azikiwe University
Teaching Hospital, Nnewi.
Email: ndukwu_ifey<@yahoo.com

Osuorah D
Child Survival Unit,
Medical Research Council UK,
the Gambia unit, Gambia.

Abstract: *Objectives:* To determine the proportion of under-5 children presenting with diarrhoeal disease, and the clinico-demographic variables associated with the outcome at the emergency paediatric ward (CHER) of the Nnamdi Azikiwe University Teaching Hospital, Nnewi, South-East Nigeria.
Methods: Clinical and demographic details of patients with diarrhoeal disease as obtained from the Paediatrics emergency ward log book over an 18month period were analyzed using SPSS and Microsoft excel software packages. The clinical variables (non-parametric) were tested for degree of association with mortality using Spearman's rank correlation. Chi square and Fischer exact test were used to determine presence of significant differences between certain variables. A p value <0.05 was deemed significant.
Results: One thousand, one hundred and sixty three out of 1,513 children admitted within the period were aged below 5 years. Acute diarrheal disease accounted for 32% and 38% respectively of morbidity and mortality in these under-five children, with a case fatality rate of 18.3%. The mean age at presentation was 11.96 months with a male to female ratio of 1.4:1. Presentation with fast breathing (Odds Ratio {OR} 2.6), convulsion (OR 2.5), loss of consciousness (OR 4.3), increased severity of dehydration, presence of one or more comorbidities (OR 4.68) and a co-diagnosis of sepsis (OR 3.23) significantly affected the outcome. (p< 0.05 in all these). Educational status of the mothers also significantly affected the outcome. (F=9.08, p=0.023)
Conclusion: Intensified effort should be made to sensitize the public about dangers of inappropriate therapy and late hospital presentation of children with diarrhoeal disease. These will reduce mortality-heralding complications.

Keywords: diarrhoeal disease; mortality; sepsis

Introduction

Diarrhoea disease remains a leading cause of childhood morbidity and mortality in developing countries like Nigeria, and is presently described as one of the two biggest child killers globally.[1,2] It trails only acute respiratory infections in the under-five mortality toll, with about 1.5 million under-five children dying each year from diarrhoea and about 80% of these deaths occurring in Africa and South Asia; India and Nigeria, topping the charts.[2,3] In effect, diarrhoeal disease presently kills more children than AIDS, malaria and measles combined.[2,4] In Nigeria, it accounts for 10% of morbidities amongst under- 5s.[5]

Diarrhoea has well defined risk factors and transmission routes with the inducing pathogens being often transmitted through consumption of contaminated food and water.[2] Though there are effective interventions for diarrhoea prevention like vaccines, promotion of early and exclusive breastfeeding, vitamin A supplementation, safe drinking water, improved sanitation; and safe effective treatment protocols such as the use of low-osmolarity oral rehydration salts (ORS) and zinc, children are still dying because these interventions are either not available or accessible to the vulnerable, especially in the developing world.[2]
When properly managed, the prognosis of diarrhoeal disease is excellent. Indeed, the mortality rate had improved significantly over the last 40 years, following global scaling up and widespread use of oral rehydration therapy.[2] Subsequently, with world attention diverted to other global emergencies, there has been a decline over the past two decades in the number of children accessing

recommended treatment for diarrhoeal disease in developing countries, with an upsurge in the number of untreated or poorly treated children who present with a spectrum of increasing severity of complications.[2,6,7] Region specific continuous evaluation of the burden and outcome of diarrhoeal disease is thus needful with highlighting of the factors that impact on prognosis, as a prerequisite to consolidate strategies that will reduce the case fatality of this highly preventable and treatable disease.

Methods

This was a retrospective study carried out in the Children Emergency Room (CHER) of the Nnamdi Azikiwe University Teaching Hospital, Nnewi. This is a Federal Government owned tertiary and referral centre of excellence in Anambra state. This hospital receives referrals from all around the state and some adjourning states like Delta and Enugu states. The CHER is manned by a full retinue of staff running 2 shifts for doctors and 3 for nurses. There are 2 consultant emergency paediatricians, 2 senior registrars during the morning shift and 1 senior registrar at night, a minimum of 1 resident doctor per shift, 2 house officers during the day shift, 1 at night, and an average of 3 nurses in each of the nursing shifts.
The study population included all patients that were admitted in CHER from January 2013 to June 2014, with acute diarrhoea. Those that were brought in dead and those with diarrhoea that had lasted more than 2 weeks were excluded. Ethical approval to study morbidities and mortalities in CHER within the time frame was obtained from the Research and Ethical Committee of the hospital. Data contained in a structured proforma was obtained from the doctors' paediatrics emergency ward log book. The CHER doctors' log contains biodemographic information on admitted patients as well as relevant clinical details like symptoms, signs, diagnoses, investigation results, initial management and outcome in the emergency room, as documented in the folders of patients, retrieved after initial stabilization of the patients.

Information extracted included the age, gender of patients, birth order, parental occupation and highest education level, presenting symptoms and duration of illness, important signs, bedside and urgent initial investigations, diagnoses and outcome. Criteria for diagnosis of acute diarrhoea in the CHER is clinical, based on the standard definition of 'an increase in daily stool fluidity, frequency and volume from what is considered normal for an individual.[2] This is made after a detailed history and thorough physical examination. The aetiological diagnosis for diarrhoea was not included in the study. Diagnoses of morbidities like malaria, sepsis and bronchopneumonia are initially made clinically, but quickly followed up by bed side, side lab and urgent main laboratory investigations. The grading of severity of dehydration was based on the current World Health Organization's clinically based criteria as no, some or severe dehydration.[8] Routinely, children presenting in this centre at the extreme of severe dehydration with signs of cardiovascular compromise and impaired organ perfusion are described as being in clinical shock.[9] Available bed side investigations include Rapid diagnostic test for malaria, urinalysis, random blood sugar. Side lab investigations include retroviral screening, packed cell volume and films for malaria parasite. Urgent main lab investigations include full blood count, serum electrolytes and chest X-ray. The diagnosis of sepsis in the CHER is based on signs of systemic inflammatory response like tachycardia, tachypnea, abnormally high or low temperature, leucocytosis and presence of presumed or confirmed infection. Data was entered in both SPSS version 16 and Microsoft Excel computer software packages. Analysis was also done using these software packages. Clinical variables were tested for degree of association with mortality using Spearman's rank correlation. Chi square test was used to determine presence of significant differences between certain variables. A p value <0.05 was deemed significant. Relevant charts, tables and figures were used to display frequency distributions of variables.

Study Results

One thousand, five hundred and thirteen children were admitted in the Children Emergency Room of the hospital within the period. There were 872 males and 641 females, with a male to female ratio of 1.4: 1. Children under 5 years of age were 1163and constituted 77% of all the patients admitted. Three hundred and seventy two of these U-5 children (214 males and 158 females) presented with acute diarrheal disease giving a prevalence of 32%, with a male to female ratio of 1.4: 1. The mean age of these children was 11.96 months ± 8.7. See Table 1 below.

Table 1: age and sex distribution of the patients

Age (months)	Male N(%)	Female N(%)	Total N(%)
1 – 11	125 (58.4)	97(61.4)	222(59.7)
12 – 35	80(37.4)	54(34.2)	134(36.0)
35 – 59	9(4.2)	7(4.4)	16(4.3)
Total	214(100)	158(100)	372(100)

Mean age is 11.96± 8.7months, Median age is 10months

Other demographic characteristics: Averagely the socioeconomic class was middle class with up to 34% of the patients being from the lowest social strata. Other details are shown in table 2.

Table 2: Demographic characteristics of patients

Characteristics	Frequency (n = 372)	Percentage (%)
Birth order		
≤4	322	86.6
>4	50	13.4
*Maternal age(years)**		
<35	298	80.2
>35	74	19.8
Maternal education		
Nil formal	3	0.6
Primary	60	16.2
Secondary	191	51.3
Tertiary	118	31.8

*0.8%(3) of the mothers were teenagers aged between 18 and 19 years

Clinical characteristics of the patients: The major presenting symptoms of the patients are illustrated in Figure 1. Most (73.9%) of the patients presented within the first week of their initial symptom, while 8.3% presented after 2 weeks of initial symptom, other than diarrhoea (acute diarrhoeal disease occurred in these ones secondarily). There was clinical dehydration at presentation in 68% (257) of them, with up to 25% of these being in clinical shock. Figure 2 is a representation of the hydration state of the patients at presentation.

Fig 1: Major presenting symptoms of the patients

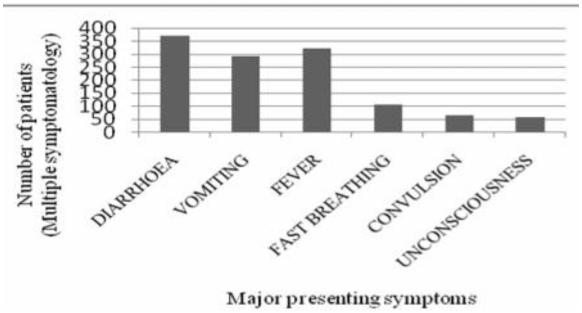
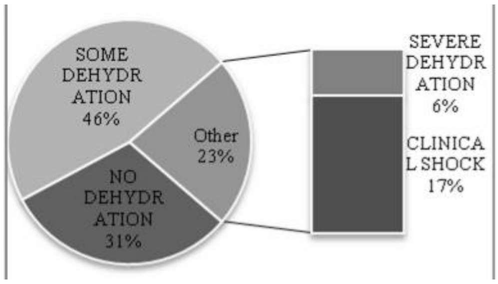
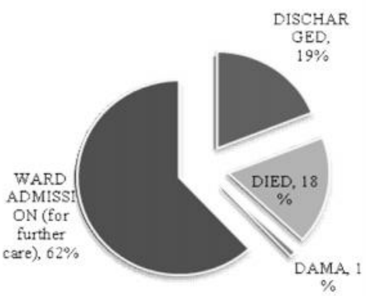


Fig 2: Levels of dehydration in the patients



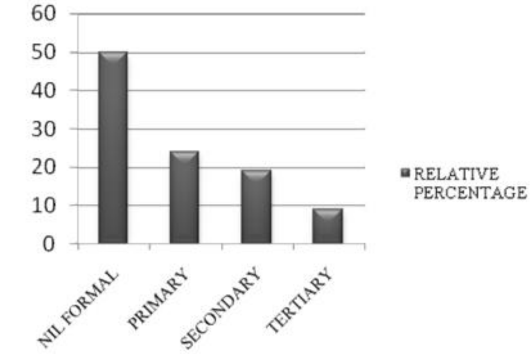
Outcome of illness: Diarrhoea disease was responsible for 38% of the 178 under-five mortalities recorded within the study period. Sixty eight of the372 children with diarrheal disease died, translating to a case fatality rate of 18%. Up to 72% of these diarrhoeal related deaths (49 of 68 patients) occurred within the first 24 hours of admission with many of them dying within minutes or few hours of presentation. The outcomes of the admissions are represented in Figure 3 below.

Fig 3: Outcome of diarrheal disease amongst under-fives



Demographic characteristics and outcome: Forty five (65%) of the children that died were infants while the rest were from 12 to 36months old. However this was not significant. (F=4.475, p=0.10). The gender of the patients also did not significantly affect the outcome. (X^2 =2.69, p= 0.10)The only demographic characteristic that had a significant relationship with the outcome was maternal education with a higher relative mortality associated with lower educational level. (F=9.08, p=0.023) See Figure 4. Bivariate analysis was equally significant at 0.01 level.

Fig 4: Relative percentage mortality per educational level



Presenting complaints and outcome

Table 3 shows the cross-tabulation of presenting symptoms with the outcome of acute diarrhoea in the children. Cconvulsions (OR 2.5, p<0.001), fast breathing (OR 2.6, p <0.001) and unconsciousness (OR 4.3, p<0.001) were significantly associated with fatal outcome in children with acute diarrheal disease. A significant strength of association with mortality in the patients was also noted with these symptoms using bivariate analysis.

Table 3: Association of clinical symptoms with mortality

Symptom	Outcome Mortality	Survived	Odd's ratio (95% ci*)	p-value
Vomiting n=293(100)	54(18.4)	239(81.6)	1.0 (0.6-1.8)	0.885
Fever n=321(100)	58(18.1)	263(81.9)	0.9 (0.5-1.7)	0.792
Convulsion** N=66(100)	24(36.4)	42(63.6)	2.5 (1.7- 3.9)	0.000
Fast breathing*** n=108(100)	35(32.4)	73(67.6)	2.6 (1.7-3.9)	0.000
Unconsciousness**** n=58(100)	30(51.7)	28(48.3)	4.3 (2.9-6.3)	0.000

* CI = confidence interval
**Spearman's correlation (0.217) significant at 0.005 level
***Spearman's correlation (0.234) significant at 0.005 level
****Spearman's correlation (0.372)significant at 0.005 level

Duration of illness and outcome: Effect of duration of illness (time of onset of initial symptom) and duration of diarrheal disease before presentation are represented on table 4 below. The patients that presented earlier had a significantlybetter outcome. (F=10.69, p<0.05;X^2 =12.24, p<0.05)

Table 4: Association between the duration of illness, diarrheal disease duration and outcome

Duration of illness	Outcome Mortality	Survived	Statistic	p-value
1-7 days n=275(100%)	40(14.5)	235(85.5)	F=10.69	0.010
8-14 days n=66(100%)	21(31.8)	45(68.2)		
15 to 30 days n=17(100%)	4(23.5)	13(76.5)		
>30 days n=14(100%)	3(21.4)	11(78.6)		
Duration of diarrheal disease				
1 day n=101(100%)	12(11.9)	89(88.1)	X^2=12.24	0.007
2 to 3 days n=121(100%)	23(19.0)	98(81.0)		
4 to 7 days n=109(100%)	18(16.5)	91(83.5)		
8 to 14 days n=38(100%)	15(36.6)	26(63.4)		

F= Fischer's exact test
X^2 = Chi square test

Presence of dehydration, other co-morbidities and outcome: The level of dehydration of these children at the time of presentation significantly affected the outcome. (F=89.43, p=0.000). Of all the patients who presented in clinical shock, 63.5% died while 14.3% and 5.3% respectively, of all those that presented with severe and some dehydration died. (See table 5) Presence of one or more co-morbidities increased the odds of dying from diarrheal disease. (OR 4.68, p=0.000). Children who had sepsis at presentation to CHER were about three times more likely to die from acute diarrhoea than those without sepsis on presentation (OR 3.23, p=0.000) (See Table 5). Bivariate analysis also showed a significant strength of association.

Table 5: Dehydration, co morbidities and outcome

Level of dehydration	Outcome Mortality	Survived	Statistic	p-value
No n=115(100)	16(13.9)	97(86.1)	F*=89.43	0.000
Some n=171(100)	9(5.2)	164(94.8)		
Severe n=21(100)	3(14.3)	18(85.7)		
Shock n=63(100)	40(63.5)	23(36.5)		
Co-morbidity			*Odd's ratio (CI)*	
One or more** n=229	60(26.2)	169(73.8)	4.68 (2.31-9.5)	0.000
Sepsis*** n=84	33(39.3)	51(60.7)	3.23 (2.15-4.87)	0.000
PEM n=28	8(28.6)	20(71.4)	1.64 (0.87-3.07)	0.143
Malaria n=48	9(18.8)	39(81.2)	1.03 (0.55-1.94)	0.928
Bronchopneumonia n=23	7(30.4)	16(69.6)	0.119 (0.90-3.36)	0.119

* Fischer's exact test
**Spearman's correlation (0.259) significant at 0.005 level
***Spearman's correlation (0.294) significant at 0.005 level

Discussion

This study showed a high burden of diarrhoeal disease morbidity and mortality amongst under-five year old children that presented to the children emergency room of the Nnamdi Azikiwe University Teaching Hospital within the study period, being responsible for about a third of morbidities and mortalities amongst them. This, alongside the high case fatality, confirms as has been documented in several studies and surveys both globally and in Nigeria in recent years, that diarrhoea remains a major cause of death in under-5 children.[1-4,10-3] In the children emergency room of another tertiary hospital in South East Nigeria, diarrhoeal disease was the commonest morbidity managed a year prior to this index study and was responsible for 43% of all mortalities within the period.[11] A hospital based study in North central Nigeria, however, documented a far less prevalence (2.7%) of diarrhoea among under-5 children.[14] The lower prevalence recorded in the study may be attributed to the larger sampling frame which included all children admitted in the Paediatric department of the tertiary Hospital over a period of 2 years unlike our study which enrolled only under-5 children admitted into the emergency unit of the Paediatric department. Their prevalence was even lower than the overall Nigerian prevalence of 10%, obtained in a national survey in which the methodology involved asking mothers about occurrence of diarrhoeal disease in the two weeks preceding the survey.[5] As diarrhoea tends to be seasonal which was noted in the same survey, these results would be largely dependent on the time of the survey.

The outcome of diarrhoeal disease in this study was worse in the children that presented with dehydration. This is not surprising as young children are known to be at great risk of life –threatening dehydration because of their high daily fluid turnover and decreased ability to conserve water like adults, thus being unlikely to tolerate increased loss of body water.[2] The past gains of the prevention of dehydration from diarrhoeal disease have not been sustained, with studies documenting a decreased awareness of the use and proper constitution of Oral Rehydration Salts (ORS).[2,12,15] In a 2010 study in South East Nigeria, while 76% of the mothers knew they should use ORS for a child with diarrhoea, only 14.2% of them could correctly prepare ORS.[15] This decreased awareness and knowledge will obviously negatively impact on the disease outcome and may be partly why diarrhoeal mortalities are soaring. Even though the mothers in our study were not questioned on their knowledge of oral rehydration, the proportion of our patients presenting with moderate and severe dehydration and shock (over 68%), with significantly increasing mortality based on severity of dehydration is highly suggestive of ignorance on the caregivers' part. Other researchers have equally documented a strong and positive correlation of a higher degree of dehydration to fatal outcome in childhood diarrhoea.[16]

Just as found in our study, children with diarrhoea who present to hospital with secondary symptoms like fast breathing and unconsciousness have been equally documented in other studies to have increased odds for mortality.[3] Known diarrhoeal complications such as electrolyte imbalance, hypoglycaemia and dehydration result in respiratory symptoms, seizures, altered consciousness and ultimately death.[16] Apart from these secondary symptoms, other conditions which are known causes of mortality in children actually co-existed with the diarrhoea disease in some of these children. This could explain the finding in this study of the presence of one or more co morbidities being significantly associated with mortality. Such findings have been documented previously.[3,12] Sepsis was the singular significant comorbidity that increased the likelihood of death from diarrhoea disease in the study children. This is not surprising as severe sepsis is a terminal event with a high fatal outcome in many infectious diseases, including diarrhoea in which clinical signs of severe sepsis with septic shock could overlap with hypovolemic shock.[3]

The significantly worse outcome seen in those with longer duration of illness has been documented in other studies.[12,17,18] This is expected because the longer lasting a diarrhoea episode is, and the longer it takes before effective and appropriate care is sought for a child with diarrhoeal disease, the more likely it is for serious and unsalvageable physiologic aberrations to set in. The poor clinical state at presentation of a significant percentage of the children in our study could be an indirect reflection of the health seeking attitude and literacy level of the population studied. This is obvious and justified by the fact that relatively, a higher percentage of children of women with lower educational attainment died. Poorly educated women are less likely to indulge in safe hygienic practices and may not recognise danger signs in ill children. It has been previously documented that Nigerian children and children from other parts of Africa are taken to health facilities when their illnesses are considered severe with obvious failure of home and other traditional therapy, contributing to late presentation to appropriate health facility.[6,12] With many of these parents influenced by cultural beliefs on the cause of and treatment of diarrhoea, alternative options including procurement of drugs prescribed by patent medicine dealers are initially exhausted.[6,12] This might explain why more than 2 out of every 10 of these index children studied presented with severe dehydration, with most of these being in shock. The functionality of the primary and secondary health care in the region, where most of the diarrhoea cases should have been initially managed, is thus compromised as many of these children are hurriedly referred to the tertiary centre verbally, as experienced in our centre, because of their critical condition.

Conclusion

Diarrhoeal disease is still a major cause of under-five morbidity and mortality. The poor clinical state of many of the index patients at presentation was associated with poor outcome of illness. Delayed presentation to hospital until there are attendant co-morbidities and complications such as severe dehydration, convulsions, fast breathing and loss of consciousness were significantly associated with increase in the odds of death. Efforts to educate caregivers about timely rehydration and early hospital presentation could reduce these mortality-heralding complications.

Authors' Contributions
CN and SO headed decision in diagnosis and management of most of the patients. CN entered and analyzed the data. CN, SO and DO drafted the manuscript. CN, SO and JE revised the manuscript.
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